8/26/04

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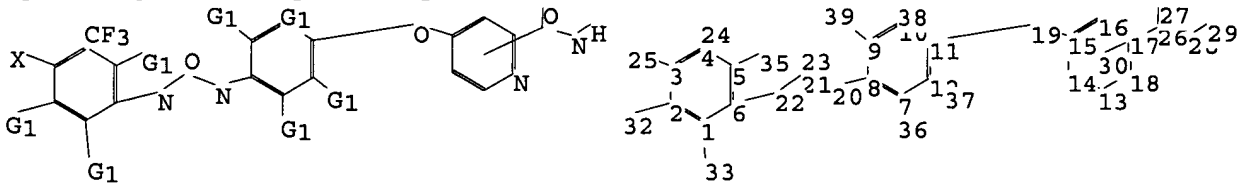

chain nodes :
19 20 21 22 23 24 25 26 27 28 29 32 33 35 36 37 38 39
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
1-33 2-32 3-25 4-24 5-35 6-22 7-36 8-20 9-39 10-38 11-19 12-37 15-19
20-21 21-22 21-23 26-27 26-28 28-29
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15
15-16 16-17 17-18
exact/norm bonds :
1-33 2-32 5-35 6-22 7-36 8-20 9-39 10-38 11-19 12-37 15-19 20-21 21-22
21-23 26-27 26-28
exact bonds :
3-25 4-24 28-29
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15
15-16 16-17 17-18

G1:H,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS 32:CLASS
33:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

8/26/04

```
=> s l1
SAMPLE SEARCH INITIATED 12:34:50 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     19 TO ITERATE

100.0% PROCESSED      19 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          119 TO      641
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 12:34:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    356 TO ITERATE

100.0% PROCESSED     356 ITERATIONS                               4 ANSWERS
SEARCH TIME: 00.00.01

L3            4 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             155.42     155.63

FILE 'CAPLUS' ENTERED AT 12:34:58 ON 26 AUG 2004
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FILE COVERS 1907 - 26 Aug 2004  VOL 141 ISS 9
FILE LAST UPDATED: 25 Aug 2004  (20040825/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4           10 L3

=> d abs bib hitstr 1-10

L4   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2004 ACS on STN
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8/26/04

AB Urea derivs. of formula A-NHCONH-B or pharmaceutically acceptable salts thereof [A = a substituted moiety of up to 40 carbon atoms of the formula -L-(M-L1)q; where L = a 5 or 6 membered cyclic structure bound directly to D; L1 = a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur; B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepared These compds. are useful for raf mediated diseases, in particular a cancerous cell growth mediated by raf kinase. All compds. exemplified, e.g. N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea, displayed IC50 of between 1 mM and 10 μM.

AN 2003:874965 CAPLUS

DN 139:364958

TI Preparation of omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

IN Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PA Bayer Corporation, USA

SO U.S. Pat. Appl. Publ., 60 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

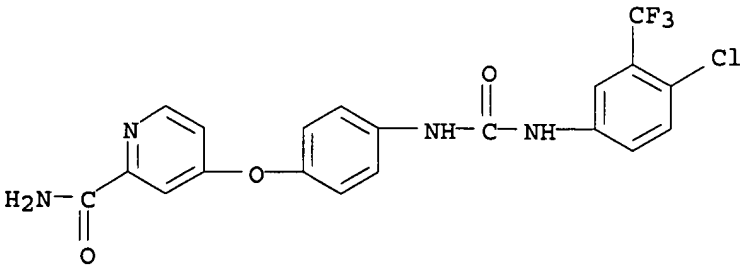
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003207872	A1	20031106	US 2002-42226	20020111
PRAI	US 2002-42226		20020111		

OS MARPAT 139:364958

IT **284461-74-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ω-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AB Aryl ureas of formula A-NHCONH-B [A = a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L1)q (where L = a 5 or 6 membered cyclic structure bound directly to D, L1 comprises a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of from 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur); B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepared These urea derivs. are useful for treating raf mediated diseases, in particular cancerous cell growth mediated by raf kinase. Thus, N-[4-bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. Thus, a solution of 4-bromo-3-(trifluoromethyl)phenyl isocyanate (8.0 g, 30.1 mmol) in CH2Cl2 (80 mL) was added dropwise to a solution of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (7.0 g, 28.8 mmol) in CH2Cl2 (40 mL) at 0°, stirred at room temperature for 16 h, and filtered to give, after washing the yellow solids, washing with CH2Cl2 (2 + 50 mL), and drying under reduced pressure (approx. 1 mmHg) at 40° to give N-[4-bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. All compds. exemplified showed IC50 between 1 nM to 10 μM against raf kinase.

AN 2003:757329 CAPLUS

DN 139:276918

TI Preparation of omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

IN Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PA Bayer Corporation, USA

SO U.S. Pat. Appl. Publ., 61 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

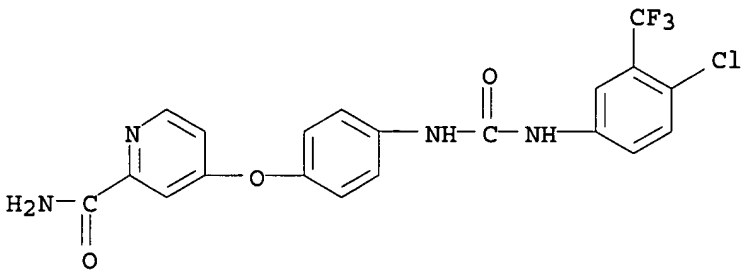
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003181442	A1	20030925	US 2001-993647	20011127
PRAI	US 2001-993647		20011127		

OS MARPAT 139:276918

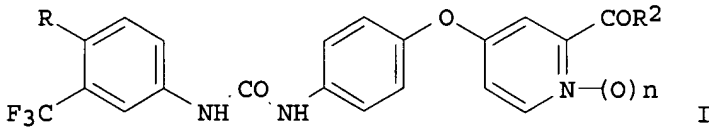
IT **284461-74-1P**, N-(4-Chloro-3-trifluoromethylphenyl)-N'-[4-[(2-carbamoyl-4-pyridyl)oxy]phenyl]urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of omega-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors and anticancer agents)

RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB Aryl ureas, such as I [R = Cl, Br; R2 = OH, NH2, NHMe, NHCH2OH, alkoxy; n = 0, 1], were prepared for use in pharmaceutical compns. for the treatment of raf kinase and p38 kinase mediated diseases. These ureas are useful for the treatment of inflammation, osteoporosis, angiogenesis disorders and hyper-proliferative disorders, such as cancer. Thus, urea I (R = Cl, R2 = NHMe, n = 1) was prepared with 57% yield by N-oxidation of I (R = Cl, R2 = NHMe, n = 0) using 3-chloroperbenzoic acid in CH2Cl2 and THF. The prepared ureas were assayed for inhibition of p38 kinase and raf kinase, as well as for cancer cell growth inhibition in human cancer cell lines, such as HCT116 and DLD-1.

AN 2003:656745 CAPLUS
DN 139:197377
TI Preparation of aryl ureas for therapeutic use as kinase inhibitors
IN Dumas, Jacques; Scott, William J.; Chien, Du-Schieng; Lee, Wendy; Bjorge, Susan; Musza, Laszlo L.; Nassar, Ala; Riedl, Bernd
PA Bayer Corporation, USA
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003068746	A1	20030821	WO 2003-US4109	20030211

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,

NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003216446 A1 20031120 US 2003-361859 20030211

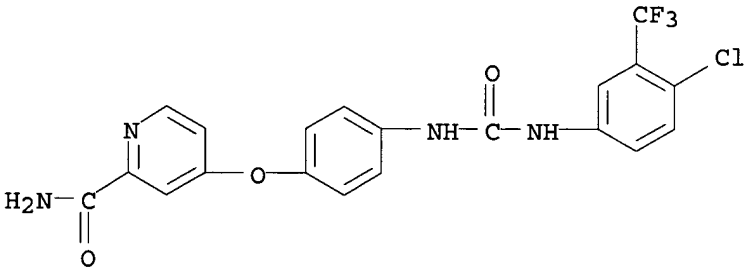
PRAI US 2002-354937P P 20020211

OS MARPAT 139:197377

IT **284461-74-1P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-carbamoyl(4-pyridyloxy)phenyl]urea **583840-04-4P** **583840-09-9P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)

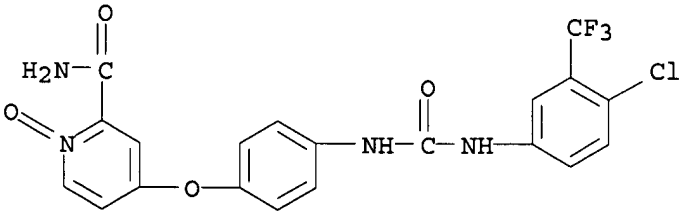
RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



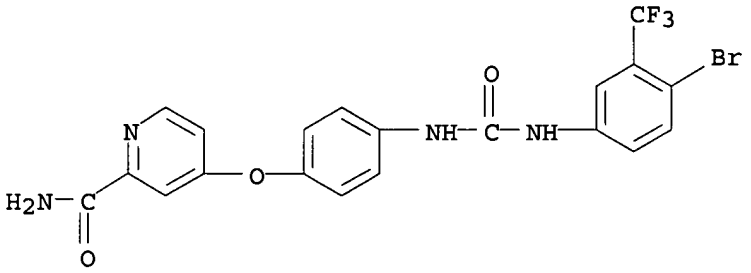
RN 583840-04-4 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, 1-oxide (9CI) (CA INDEX NAME)

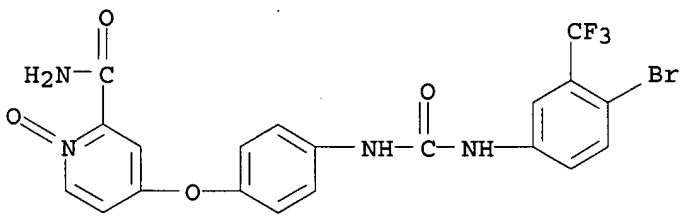


RN 583840-09-9 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)

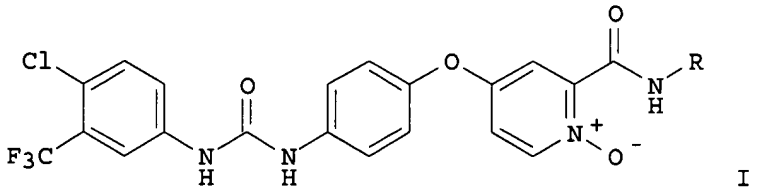


IT **583840-08-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)
RN 583840-08-8 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-bromo-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, 1-oxide (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I

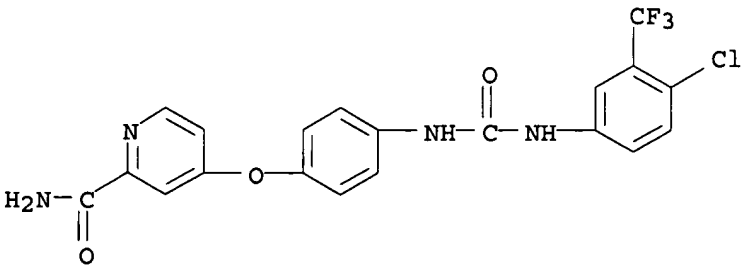
AB The title ureas containing a pyridine, quinoline, or isoquinoline functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH2)mO(CH2)l, (CH2)m(CH2)l, (CH2)mCO(CH2)l, etc.; m, l = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide,

isoquinoline-1-oxide; with the provisos] which are useful in the treatment of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Preparation of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical composition comprising the title ureas was claimed.

AN 2003:656581 CAPLUS
DN 139:197370
TI Preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors
IN Dumas, Jacques; Scott, William J.; Riedl, Bernd
PA Bayer Corporation, USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

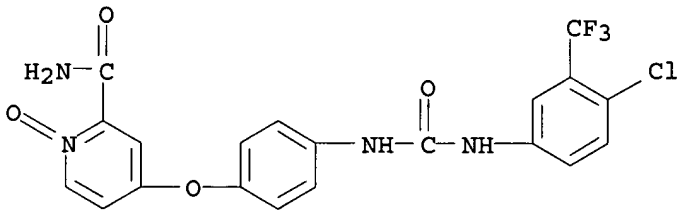
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003068229	A1	20030821	WO 2003-US4110	20030211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003216396	A1	20031120	US 2003-361850	20030211
PRAI US 2002-354935P	P	20020211		

OS MARPAT 139:197370
IT **284461-74-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors)
RN 284461-74-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



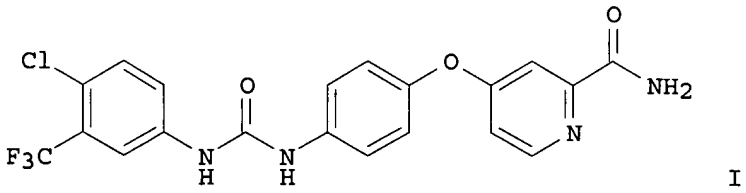
8/26/04

IT **583840-04-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors)
RN 583840-04-4 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-, 1-oxide (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB The title compds. ANHCONHB [A, B = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, etc.], useful for treating diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Prepns. of three title ureas are described. E.g., a 3-step synthesis of the urea I (starting from Me 4-chloro-2-pyridinecarboxylate hydrochloride), was given. The KDR (VEGFR2) assay for testing the title ureas is described.
AN 2003:656580 CAPLUS
DN 139:197369
TI Preparation of aryl ureas with angiogenesis inhibiting activity
IN Dumas, Jacques; Scott, William J.; Elting, James; Hatoum-Makdad, Holia
PA Bayer Corporation, USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003068228	A1	20030821	WO 2003-US4103	20030211

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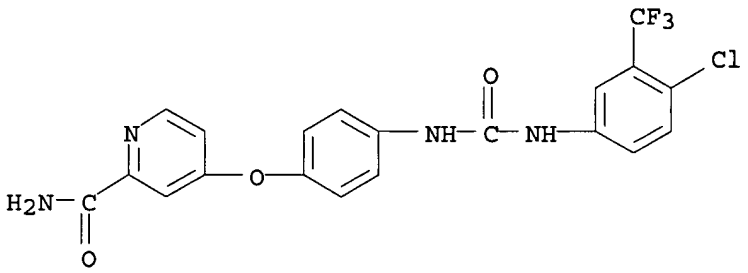
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003207870 A1 20031106 US 2003-361858 20030211
PRAI US 2002-354950P P 20020211
OS MARPAT 139:197369
IT **284461-74-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl ureas with angiogenesis inhibiting activity)
RN 284461-74-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

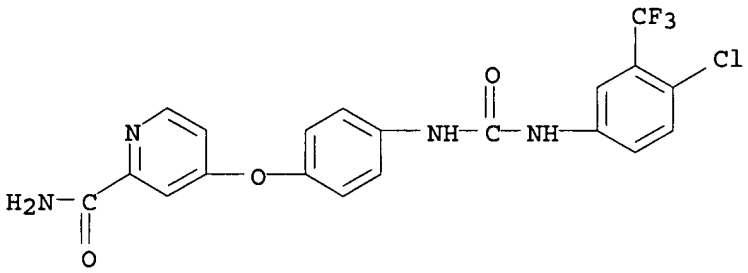
L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
AB ADB [I; D = NHCONH; A = L(ML1)q; L = 5-6 membered cyclic structure bound directly to D; L1 = substituted cyclic moiety having ≥5 members, M = bridging group having ≥1 atom; q = 1-3; L, L1 contain 0-4 N, O, S; B = (substituted) up to tricyclic aryl, heteroaryl of ≤30 C atoms with ≥1 6-membered cyclic structure bound directly to D containing 0-4 N, O, S], were prepared Thus, 4-chloro-3-(trifluoromethyl)phenyl isocyanate in CH2Cl2 was added dropwise to a suspension of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (preparation given) in CH2Cl2 at 0°; the resulting mixture was stirred at room temperature for 22 h. to afford N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. I inhibited RAF kinase in the range 1 nM-1 μM. I pharmaceutical compns. are claimed.
AN 2003:590832 CAPLUS
DN 139:149528
TI Preparation of diphenylureas as RAF kinase inhibitors
IN Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

8/26/04

PA Bayer Corporation, USA
SO U.S. Pat. Appl. Publ., 62 pp., Cont. of U. S. Ser. No. 42,203.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003144278	A1	20030731	US 2002-283248	20021030
PRAI US 2001-367380P	P	20010112		
US 2002-42203	A1	20020111		

OS MARPAT 139:149528
IT **284461-74-1P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridylox y)phenyl]urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diphenylureas as RAF kinase inhibitors)
RN 284461-74-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
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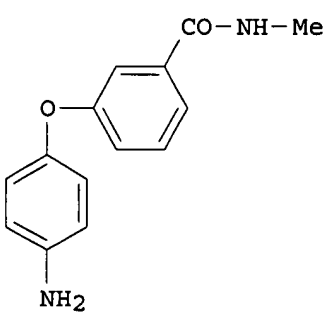

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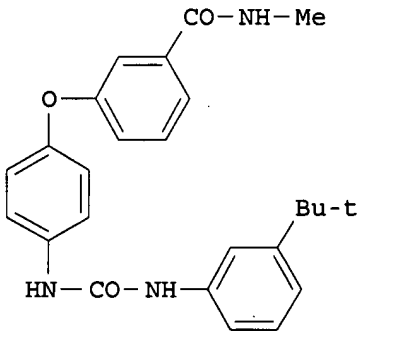

III

AB Title compds. B-NHCONH-L-(M-L1)q (I) [B = (un)substituted pyridyl, quinolinyl, isoquinolinyl; L = 5 or 6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; with proviso that L and L1 contain 0-4 hetero atoms, e.g., N, O and S] and their pharmaceutically acceptable salts were prepared For example, coupling of aniline II, e.g., prepared from Et 3-hydroxybenzoate in 4-steps, with bis(trichloromethyl)carbonate followed by 3-tert-butylaniline afforded urea III. In in vitro raf kinase assays, 112-specific examples of compds. I inhibited kinase activity with IC50 values ranging from 10 nM-10 μM. Compds. I are useful for the treatment of cancerous cell growth mediated by raf kinase.

AN 2002:850357 CAPLUS

DN 137:352907

TI Preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase for the treatment of tumors and/or cancerous cell growth

IN Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Robert, Sibley N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.

PA Bayer Corporation, USA

SO U.S. Pat. Appl. Publ., 63 pp., Cont.-in-part of U.S. Ser. No. 758,548.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002165394	A1	20021107	US 2001-777920	20010207
	ZA 2001005751	A	20030714	ZA 2001-5751	20010712
	US 2002137774	A1	20020926	US 2001-907970	20010719
	WO 2002062763	A2	20020815	WO 2002-US3361	20020207
	WO 2002062763	A3	20021010		
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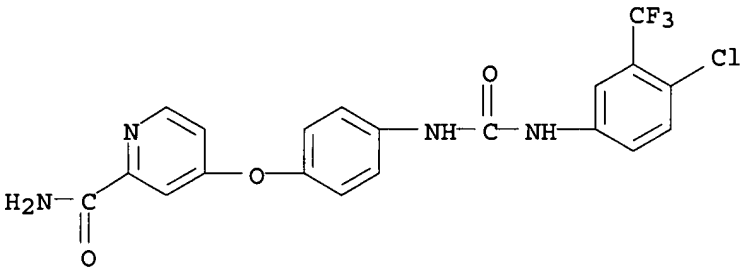
	US 2003139605	A1	20030724	US 2002-71248	20020211
PRAI	US 1999-115877P	P	19990113		
	US 1999-257266	B2	19990225		
	US 1999-425228	B2	19991022		
	US 2001-758548	A2	20010112		
	US 1999-115878P	P	19990113		
	US 2001-777920	A	20010207		
	US 2001-948915	A1	20010910		

OS MARPAT 137:352907

IT **284461-74-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase)

RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
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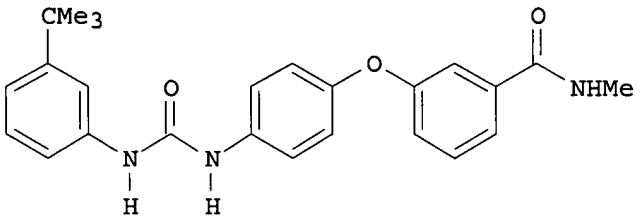

II

AB Title compds., e.g., RNHCONHZOR1 [I; R = C6H4(CMe3)-3, 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepared Thus, 4-(H2N)C6H4OC6H4(CONHMe)-4 (preparation given) was condensed with 3-(Me3C)C6H4NH2 and CO(OCCl3)2 to give title compound II. Data for biol. activity of title compds. were given.

AN 2002:615574 CAPLUS

DN 137:169425

TI Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors

IN Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.

PA Bayer Corporation, USA

SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002062763	A2	20020815	WO 2002-US3361	20020207
	WO 2002062763	A3	20021010		

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
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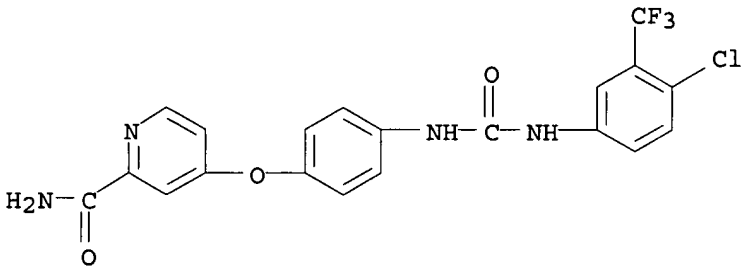
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002165394 A1 20021107 US 2001-777920 20010207
PRAI US 2001-777920 A 20010207
US 1999-115877P P 19990113
US 1999-257266 B2 19990225
US 1999-425228 B2 19991022
US 2001-758548 A2 20010112
OS MARPAT 137:169425
IT **284461-74-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)
RN 284461-74-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
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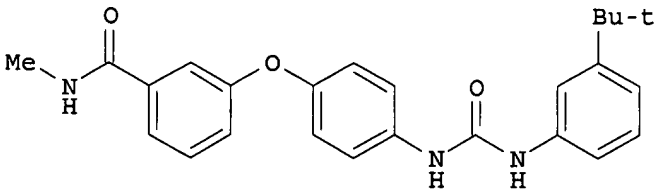

II

AB This invention relates to the preparation and use of (hetero)aryl ureas ANHCONHB [I; A = L(ML1)q; L = 5- or 6-membered (hetero)aryl, especially Ph or pyridinyl; M = bridging group; L1 = (hetero)aryl with at least one (un)substituted sulfamoyl, carboxy, or carbamoyl substituent; q = 1-3; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] for

the treatment of raf mediated diseases, such as cancer (no data). Approx. 100 invention compds. and numerous intermediates were prepared For instance, 3-tert-butylaniline was coupled with bis(trichloromethyl)carbonate to form the isocyanate, followed by addition of 4-(3-N-methylcarbamoylphenoxy)aniline (preparation given) to afford the urea II.

AN 2000:493516 CAPLUS
DN 133:120157
TI Preparation of ω-carboxy(hetero)aryl substituted diphenyl ureas as raf kinase inhibitors
IN Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.
PA Bayer Corporation, USA
SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000042012	A1	20000720	WO 2000-US648	20000112
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2359510	AA	20000720	CA 2000-2359510	20000112
	AU 2000025016	A5	20000801	AU 2000-25016	20000112
	EP 1140840	A1	20011010	EP 2000-903239	20000112
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	EE 200100368	A	20030415	EE 2001-368	20000112
	JP 2003526613	T2	20030909	JP 2000-593580	20000112
	BR 2000007487	A	20030923	BR 2000-7487	20000112
	US 2001011135	A1	20010802	US 2001-773659	20010202
	US 2001011136	A1	20010802	US 2001-773675	20010202
	US 2001016659	A1	20010823	US 2001-773672	20010202
	US 2001027202	A1	20011004	US 2001-773658	20010202
	US 2001034447	A1	20011025	US 2001-773604	20010202
	NO 2001003463	A	20010912	NO 2001-3463	20010712
	ZA 2001005751	A	20030714	ZA 2001-5751	20010712
	US 2002137774	A1	20020926	US 2001-907970	20010719
	BG 105763	A	20020329	BG 2001-105763	20010801
	HR 2001000580	A1	20020831	HR 2001-580	20010802
	US 2002042517	A1	20020411	US 2001-948915	20010910
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PRAI	US 1999-115877P	P	19990113		
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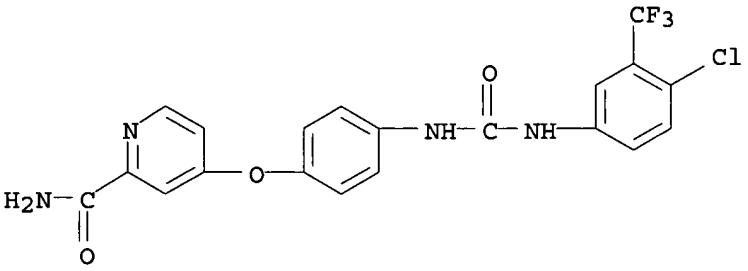
	US 1999-425228	A2	19991022		
	US 1999-115878P	P	19990113		
	WO 2000-US648	W	20000112		
	US 2001-948915	A1	20010910		

OS MARPAT 133:120157
IT **284461-74-1P**, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-

carbamoyl-4-pyridyloxy)phenyl]urea
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of ω-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

RN 284461-74-1 CAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

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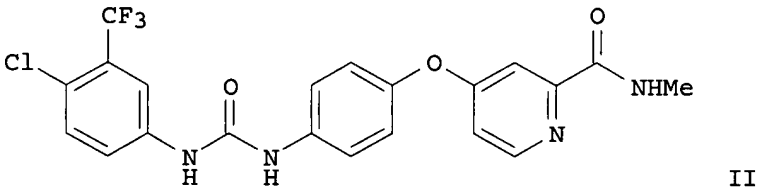

II

AB The title compds. ADB [I; D = NHCONH; A = substituted moiety of up to 40 carbon atoms of the formula L(ML1)q (wherein L = 5-6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having al least one atom; q = 1-3; each of L and L1 contains 0-4 members of the group consisting of N, O and S); B = (un)substituted up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of N, O and S], useful in treating p38 mediated diseases, were prepared E.g., a multi-step synthesis of the urea II which showed IC50 of 1-10 μM against p38, was given. Compds. I are effective at 0.01-200 mg/kg/day (oral administration).

AN 2000:493376 CAPLUS

DN 133:120155

TI Preparation of ω-carboxy aryl substituted diphenyl ureas as p38 kinase inhibitors

IN Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott,

William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.
PA Bayer Corporation, USA
SO PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000041698	A1	20000720	WO 2000-US768	20000113
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	US 2003105091	A1	20030605	US 2002-86417	20020304
PRAI	US 1999-115878P	P	19990113		
	US 1999-257265	A2	19990225		
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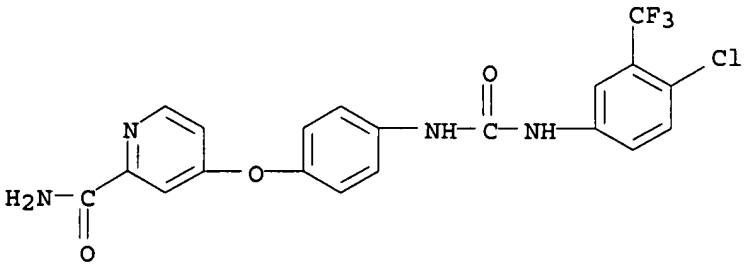
	US 2001-948915	A1	20010910		

OS MARPAT 133:120155
IT **284461-74-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ω-carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)
RN 284461-74-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



8/26/04

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	52.00	207.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.00	-7.00

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Property values tagged with IC are from the ZIC/VINITI data file
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DICTIONARY FILE UPDATES: 25 AUG 2004 HIGHEST RN 732955-11-2

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Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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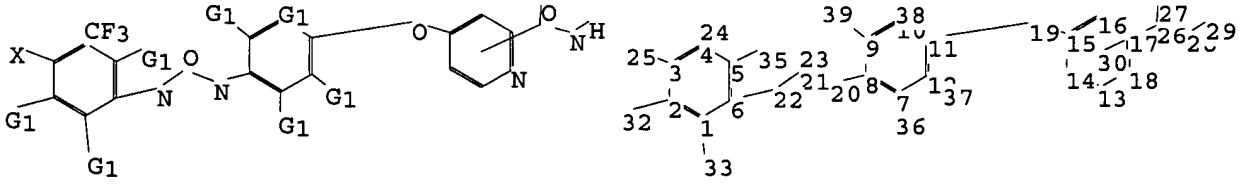

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ring nodes :
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ring bonds :

10071248

8/26/04

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14-15
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exact bonds :
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normalized bonds :
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G1:H,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
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L5 STR

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Structure attributes must be viewed using STN Express query preparation.

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8/26/04

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